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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/819,946	03/28/2001	D. Wade Walke	LEX-0157-USA	2952

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EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	**PAPER NUMBER**
1646	11

DATE MAILED: 01/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/819,946	Applicant(s) Walke et al.
	Examiner Michael Brannock	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 22, 2002* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-3, 6, and 7* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3, 6, and 7* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of Application: Claims and Amendments

1. Claims 1-3 and new claims 6 and 7 are pending and currently under examination.

2. Applicant is notified that the amendments put forth in Paper 10, 11/17/02, have been entered in full.

3. Applicant is notified that any outstanding rejection/objection, that is not expressly maintained in this Office action, has been withdrawn.

4.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 2 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, as set forth previously.

Claim 2 requires that the nucleic acid hybridize under stringent conditions. The term "stringent conditions" is confusing because it is a relative term and encompasses conditions of varying degrees of stringency - such conditions determining the bounds of the claim. However, the art does not provide an unambiguous definition of the term "stringent conditions" and neither is such a definition given for the term in the specification which puts forth the metes and bounds

of the claim Applicant is seeking protection for. The specification defines the term by way of examples at page 8, however, examples are insufficient to establish the metes and bounds of a claim.

Applicant argues that the claims have been amended to recite "highly stringent conditions", which is defined in the specification at page 8. This argument has been fully considered but not deemed persuasive. The phrase "highly stringent conditions" is a relative phrase, and, as set forth above and previously, the phrase is defined by way of example in the specification, see page 8, line 12, wherein the recited conditions are indicated to be an example of "highly stringent conditions" ("e.g." is an abbreviation of the Latin phrase *exempli gratia*, which means "for example"). The metes and bounds of a phrase that denotes relative meaning, such as "highly stringent conditions", cannot be defined by examples. Thus the metes and bounds of the claim cannot be determined.

It is again suggested that the claim recite the actual conditions that applicant considers to be stringent, i.e., salt concentration and temperature conditions of incubations and washes.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 1-3 and new claims 6 and 7 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility, as set forth previously and reiterated, in full, below. The claims are directed to polynucleotides of SEQ ID NO: 1 encoding polypeptides of SEQ ID NO: 2 The instant specification puts forth that the polypeptide is useful in a screening method to determine what ligands may activate or inhibit the polypeptide and also to determine what the physiological effects of the polypeptide might be (see page 1 and 4, for example). This proposed use lacks a specific and substantial utility. It is not a specific use because any integral membrane protein could be used in exactly the same way. Further, many polypeptides are known in the art, yet the polypeptides have no known function or known ligands. Any of these orphan clones could be used in the manner described in the specification for the claimed polypeptide.

Furthermore, the proposed use of the polypeptide to screen for ligands of the polypeptide or for biologic effects of the polypeptide is not a substantial utility. A substantial utility is a practical use which amounts to more than a starting point for further research and investigation and does not require or constitute carrying out further research to identify or reasonably confirm what the practical use might ultimately be. For example, an assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would be a practical use of the material. However, a method of treating an unspecified disease or condition with a material that has no particular correlation with a disease would not constitute a substantial utility. Basic research, such as studying the properties of the claimed

product or the mechanisms in which the product is involved, does not constitute a substantial utility.

The specification puts forth that the polypeptide could be involved in any number of disparate disease states, and could therefore be used as a diagnostic (page 6 and 33, for example) or therapeutic agent (see page 7 and 18, for example). A stated belief that a correlation exists between the polypeptides and any number of diseases is not sufficient guidance to use the claimed polynucleotides to treat and/or diagnosis a particular disease; it merely defines a starting point for further research and investigation.

The specification puts forth that the polynucleotides and polypeptides could be used as tissue specific or chromosomal markers, page 10. Consistent with current examination guidelines, use as a tissue specific and/or chromosomal marker is not considered to be a substantial utility. Most every polypeptide exhibits some tissue specific pattern of expression and most every gene encoding a polypeptide is localized to some region of a chromosome. However, without some assertion that the tissue or chromosomal localization can be used to practice a particular substantial utility, as in a marker for a particular disease state, the use of the polypeptides or polynucleotides as tissue or chromosomal marker does not constitute a substantial utility.

The specification puts forth that the polypeptide and/or polynucleotides could be used in forensic biology (page 37). However the specification does not teach that any particular nucleic acid or amino acid sequence is distinctive of any individual. While one of skill in the art would

appreciate that there may exist polymorphisms in the disclosed sequences, this amounts to nothing more than an invitation to the skilled artisan to try and find such polypmorphisms if they exist.

The specification puts that the polypeptide has similarity to known taste, pheromone, calcium sensing, peptide hormone, and glutamate receptors (page 5), however the specification does not appear to assert that the polypeptide has any particular functional properties. The specification asserts that the polypeptide or polynucleotide could be used as part of a micro-array for toxicology testing, drug screening, and pharmacogenomics (see pages 11 and 14). These purposed uses are not substantial utilities because each use amounts to no more than an invitation to study the properties of the polynucleotide or polypeptides, e.g. to determine whether a compound alters the expression of the polypeptide, and then to determine what, if any, the consequence of that alteration may be, or also to determine what ligands might bind to the polypeptide, e.g. drug screening. Such an invitation to perform research on the claimed polynucleotide is not a substantial utility.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific or substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids.

Applicant argues the instant polynucleotides encode a GPCR and that most drugs target GPCRs, thus membership in the group of GPCRs confers a specific, substantial credible well-

established utility. Citing case law, Applicant argues that the threshold for utility is low. his argument has been fully considered but not deemed persuasive. The specification has not asserted a utility that is specific to the instant molecule, the asserted utilities are based on any use that is common to all members of the GPCR family, yet importantly, there does not appear to be any particular use, common among the GPCR family members, that amounts to a substantial utility. There does not appear to be a common property that GPCRs share, and that any new member might also be expected to possess, that could be exploited in a manner that could be considered a substantial utility under 35 U.S.C. § 101. Each asserted use, e.g. drug screening, expression profiling, toxicology testing, etc., being based on the common properties of GPCRs, amounts to no more than an invitation to the skilled artisan to take the polypeptides and try to find if any drugs bind the polypeptides, or try to find any correlation between the expression of the polypeptides and the administration of any particular drug, or to see if there is a correlation between the expression of the polypeptides and the onset of any particular disease. While this type of basic research is recognized in the "real world" it cannot, alone, be the basis of a patent. Applicant's asserted utilities are essentially a call to perform such research and investigation; and, as set forth previously, such basic research as studying the properties of the claimed product or the mechanisms in which the product is involved does not constitute a substantial utility. Thus, the asserted utilities are not specific to the claimed molecules and nor are the utilities substantial because each requires extensive experimentation to try to find a way, ultimately, to use the molecules.

Applicant further argues that the instant polypeptide is a taste receptor, and thus has a specific and well established utility. This argument has been fully considered but not deemed persuasive. First, the examiner can find no assertion in the specification that the polypeptide is a taste receptor. Second, knowledge that the polypeptide is a taste receptor does not provide the artisan with sufficient knowledge as to how to immediately use the polypeptide in any way that provides a substantial utility. Using the information provided by instant disclosure and by the prior art, the artisan might then begin a research plan to determine what particular properties the protein has, e.g. to try to find what tastants bind to the protein, or determine how the protein is involved in the perception of taste, so as to ultimately learn how to use the protein. The specification provides no guidance as to how to use the protein based on any property relating to taste. The specification merely asserts that the polypeptide has homology to known receptors having disparate functions and properties, e.g. taste, pheromone, calcium sensing, peptide hormone, and glutamate receptors (page 5). Thus, the question at issue is whether or not the broad general assertion that the claimed nucleic acids might be used for *some* diagnostic application in the absence of a disclosure of *which* diagnostic application would be considered to be an assertion of a specific, substantial, and credible utility. For reasons set forth above the disclosure satisfies none of the three criteria *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the

usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.')

Applicant's reliance on *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995) is misplaced. That court decision determined that a compound which belonged to a family of compounds known to have anti-tumor activity, which is a common and well established utility for that family of compounds, would be reasonably expected to have anti-tumor activity in light of positive in vitro data with respect to that particular compound since that data has proven to be an indicator of anti-cancer activity by other members of that family. As indicated above, the protein of the instant invention does not belong to a family of compounds with a common well established specific and substantial utility. The utility of a particular member of the receptor family, to which the protein in the instant application belongs, lies in the knowledge that the particular member modulates a specific physiological activity in response to a specific ligand or involved in a particular disease or some other phenotype. Since the instant specification does not disclose the identity of a native ligand for the instant protein nor the identity of the pathway through which that receptor transduces it signal in response to that ligand, nor any other particular phenotype associated with the polynucleotide or the protein, the instant claimed polynucleotide is not particularly useful.

Applicant argues from the stand point that the requirement for some experimentation to practice the invention does not negate the utility requirement. This argument has been fully

considered but not deemed persuasive. The issue is not that some experimentation is required to use the polypeptide in a particular asserted way; the issue is that, in the instant case, experimentation is required to try to find a way to particularly use the polypeptide, such experimentation, itself, being the asserted use and also being merely a starting point for research and investigation.

Applicant argues that the use of polynucleotides and polypeptides, such as that of the instant invention, is well established in the field of microarray technology (e.g. gene chips). This argument has been fully considered but not deemed persuasive. It is agreed that microarray technology has patentable utility. However, the microarray is not being claimed, but rather a polynucleotide that can be used in microarrays. The claimed polynucleotide is not disclosed as being expressed at an altered level or form in any diseased tissue as compared to the corresponding healthy tissue. The claimed polynucleotide is not disclosed as being expressed at an altered level or form under any set of conditions or being correlated with any particular phenotype. Nor has there been any assertion of any particular effect or outcome that may be discerned from the presence of the polynucleotide in a gene chip. Therefore, the assertion that the claimed polynucleotide has patentable utility as a probe in, or member of, a microarray is not specific. Any orphan polynucleotide can be used in the same way.

Applicant refers to other publications and patents that discuss microarrays and gene expression technology with respect to drug screening and toxicology testing. Again, this is not found to be persuasive, because the arguments and evidence merely show that microarray

technology is important and useful to the scientific community. These publications do not show that the claimed invention has a patentable utility. The use of the claimed uncharacterized polynucleotides in such studies would have provided no more information than the use of any other polynucleotide encoding an orphan protein. The asserted utility for the claimed polynucleotide is not specific to the claimed polynucleotide. Due to the lack of disclosure of a correlation between the claimed polynucleotides and a particular disorder, or any particularly useful phenotype, the asserted utility is also not substantial, as discussed above.

Applicant argues, essentially, that any polynucleotide known to comprise an exon would have credible and substantial utility in the analysis of genomic data. Again, this is a utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins. Neither Applicant's cited references nor the instant specification appear to assert a use that amounts to a substantial utility. The skilled artisan appreciates that Applicant's asserted uses for the polynucleotide, e.g. in the analysis of how the gene is transcribed and/or organized is simply a study of the properties of the claimed nucleic acid. As set forth previously, such basic research as studying the properties of the claimed product or the mechanisms in which the product is involved does not constitute a substantial utility.

Applicant argues, essentially, that a "real-world" utility exists if actual use or commercial success can be shown. Citing case law, Applicant argues that thousands of venture capitalists and the scientific community have acknowledged the value genomic data, and that databases that included the claimed polynucleotide would be even more valuable. Applicant's arguments have

been fully considered but are not deemed to be persuasive. The case law indicates that a rejection under 35 U.S.C. § 101 *for lack of operability* can be overcome by a showing of actual use or commercial success. The instant issue is whether or not the asserted utilities meet the three-pronged test for credibility, specificity, and substantiality. Such is not necessarily addressed by a showing of commercial success or actual use. Many products which lack patentable utility enjoy commercial success, are actually used, and are considered valuable. These include silly fads such as pet rocks, but also include serious scientific products like orphan receptors.

Applicant argues that other patents have issued wherein similar assertions of utility have been made. This argument has been fully considered but not deemed persuasive. It is the instant application that is currently under examination. This Application is being examined based on the current examination guidelines.

Applicant argues (pg 8) that the legal test for utility is simply an assessment of credibility. This argument has been fully considered but not deemed persuasive. The current examination guidelines, to which Applicant refers, clearly indicate that the credible utility must be a specific and substantial utility. As set forth above, the asserted uses, provided in the specification, are not specific or otherwise substantial utilities.

Applicant challenges the examiner's questioning that polymorphisms of the polynucleotide exist. Applicant's argument is well taken, in part. One skilled in the art would certainly expect that natural polymorphisms (e.g. SNPs) exist for any naturally occurring polynucleotide. The

issues, as set forth previously, are (1) that the specification does not teach that any particular nucleic acid or amino acid sequence is distinctive of any individual. (2)While one of skill in the art would appreciate that there may exist polymorphisms in the disclosed sequences, this amounts to nothing more than an invitation to the skilled artisan to try and find such polypmorphisms and then to determine any consequence of these polymorphisims. This use is not specific because any naturally occurring polynucleotide could be used in the same way. It is not substantial because it is simply an invitation to try to find polymorphisms and then to try to find correlations between them and any phenomena. (3) Additionally, as set forth previously, it is unclear it the polymorphisms disclosed in the specification are naturally occurring or are artifacts of the cloning and sequencing procedures. The skilled artisan would therefore appreciate that the instant disclosure of such polymorphisms simply presents an invitation to the artisan to investigate the claimed polynucleotides to try to determine if such polymorphisms are indicative of any human individual or of any phenomena that could be further exploited.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 are also rejected under 35 U.S.C. § 112 first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well

established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation, as set forth previously. It is noted that the claims have been amended to require that the polynucleotide encode the full length SEQ ID NO: 2.

Conclusion

10. No claims are allowable.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Thursdays from 8:00 a.m. to 5:30 p.m.

The examiner can also normally be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

January 9, 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600